REMARKS UNDER 37 CFR § 1.115

FORMAL MATTERS

Claims 85-131 are pending after entry of the amendments set forth herein.

Claims 85-93, 95, 96, 111, and 117 are amended. Claim 85 has been amended to recite the nature of the modulation and Claim 85 has been further amended to define GPCR. Support for these amendments may be found in Applicants' specification, for example at page 37, lines 4 and 5 and at page 1, second paragraph, respectively. Claim 86 has been amended to recite that the modulator of cardioprotection is a modulator of cardiomyocyte survival or cardiomyocyte apoptosis. Support for this change may be found, for example, at page 52, lines 5-7, in Examples 16 and 17 at pages 76 and 77, and at page 4, lines 8 and 9 of Applicants' specification. In addition, Claims 85 and 88 have been amended to recite three additional members to the Markush group of receptors. Support for this change may be found at page 6, lines 1 and 2; at page 22, lines 23 and 24; and at page 81, lines 2-6. Claims 87, 89-93, 95, and 96 have been made multiply dependent. Editorial changes have been made in claims 87, 88 and 111, and 177, and further claim 117 has been made dependent upon claim 85. Support for the change to claim 117 may be found, for example, at page 32, first complete paragraph.

New claims 122-131 have been added. Support for these claims may be found in Applicants' specification, for example at page 22, last paragraph to page 23, second paragraph; page 26, lines 17 and 18; page 36, first paragraph; page 48, first complete paragraph; page 56, line 31; and page 64, line 29.

No new matter has been added.

RESTRICTION REQUIREMENT

The Examiner has required restriction of one group from among fourteen recited groups (I-XIV), and further has required an election of a single amino acid species and a single disease species recited in Claims 89-91 and 106-108.

Applicants hereby elect **with traverse** to prosecute the invention of Group I, the species of SEQ ID NO:3, and congestive heart failure as the disease species.

The standard for Unity of Invention is set forth in 37 C.F.R. § 1.475 as follows (emphasis added):

§ 1.475 Unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage.

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. **The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art**.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

* * *

(e) **The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim**.

The present application is a national stage application under 35 U.S.C. § 371. Accordingly, the present application is entitled to the application of the above Unity of Invention standard.

The Restriction Requirement is based on an erroneously drawn special technical feature

The Examiner has asserted that the special technical feature linking Groups I-XIV is a polypeptide of RUP41 GPCR. However, the Examiner has asserted further that because the amino acid sequence of SEQ ID NO:2 is disclosed in the art (in U.S. Patent 6,555,339 to Behan et al.), it does not define a contribution over the prior art, and therefore does not constitute a special technical feature that would lead to unity of invention.

Applicants respectfully disagree. The special technical feature is not the polypeptide of RUP41 GPCR. Rather, Applicants have discovered and claimed an association of certain RUP41 polypeptides and variants thereof with cardioprotection. It is this discovery that constitutes a special technical feature of the present claims. Such an association does in fact define a contribution over the prior art, and would constitute a special technical feature that would lead to unity of invention, at least with respect to Groups I-VI and XI. Accordingly, these Groups should be rejoined, which action is respectfully requested.

The amino acid sequences recited in the claims share a significant structural element and thus do not form a proper basis for restriction

The Examiner has also asserted that each amino acid sequence recited in Applicants' claims represents an additional inventive group, and has required an election of one such sequence. Such a determination appears to be an erroneous conclusion unsupported by any reason or rationale.

The amino acid sequence in Applicants' claims are recited in Markush group format. MPEP § 1893.03(d) states that a single inventive concept is present between/among different embodiments if a common structure is present in all of the embodiments. By way of example, MPEP § 1850 III. B(1), which is concerned with Markush practice vis-à-vis unity of invention, states that different alternative chemical compounds, as long as they all share a significant structural element, should be examined together. In addition, MPEP § 1850 III. B(2), which is also concerned with Markush practice vis-à-vis unity of invention, states that in cases where the common structure cannot be the unifying criteria, if all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains, the alternatives should be examined together.

A significant structural element is shared by all of the alternatives where the compounds share a common chemical structure which occupies a large portion of their structures or, in the situation where compounds have in common only a small portion of their structures, the commonly shared structure

constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. See MPEP § 1850 III. B(2). The structural element may be a single component or a combination of individual components linked together. *Ibid.*

The amino sequences recited in Applicants' claims are closely related. The amino acid sequences set forth in step (a)(ii-iv) of Claim 85, for example, are >99% identical to SEQ ID NO:2; the amino acid sequence of step (a)(vi) is about 95% identical to SEQ ID NO:2, and the amino acid of step (a)(v) is an allele of SEQ ID NO:2. As such, Applicants submit that the polypeptides recited in the claims share a significant structural element, and that therefore there is unity of invention under PCT Rule 13.1 among the members of the Markush group. Accordingly, the requirement for an election of one member (species) of the Markush group is improper and should be withdrawn.

The election of species relating to diseases recited in the claims is improper as these share the special technical feature of RUP41 GPCR's association with cardioprotection

The Examiner's requirement for election of a single disease species is improper. In the instant case, the species are disclosed in Markush format and all of the members of the Markush groups are agents that would effect their activity through stimulating the RUP41 GPCR. In addition, each of the recited diseases are those that are amenable to treatment or prevention by providing for cardioprotection in the subject. Therefore, the agents suitable for prevention or treatment of the diseases listed in the claims are linked by the same special technical feature as discussed above: namely, the discovery that the RUP41 GPCR is associated with cardioprotection. Thus, for example, as set out in Claim 88, agents for prevention or treatment of a cardiovascular disorder, agents for prevention or treatment of an ischemic heart disease, and agents for effecting a change in cardiovascular function are linked in that they stimulate RUP41 GPCR.

As such, Applicants submit that there is unity of invention under PCT Rule 13.1 among the members of the Markush groups. Accordingly, the requirement for an election of one member (species) from the claimed Markush groups is improper and should be withdrawn.

Request for rejoinder of Groups I-VI and XI; Groups VII and VIII; and Groups XIII and XI

Moreover, Applicants submit that certain of the Groups I-XIV should be rejoined with each other because there is unity of invention in the subject matter of these groups. Specifically, Applicants request

rejoinder of Groups I-VI and XI, Groups VII and VIII, and Groups XIII and XIV for the following reasons:

Groups I and XI should be rejoined because a potential modulator can be a potential ligand and vice versa. Note that Applicants define *allosteric modulators* at page 32 of the specification to mean ligands, for example. See also the definitions of *ligand* and *modulate* at page 37. One may see from these definitions that a modulator is a molecule that increases or decreases the amount, quality, or effect of a particular activity, function, or molecule. A *ligand* is defined as a molecule specific for a naturally occurring receptor. This definition refers only to the binding specificity of ligand and receptor and not to the effect that may result from binding of the ligand to the receptor. Thus, a ligand may act, for example, as an agonist, as an antagonist, or as a modulator after binding to the receptor.

Furthermore, as pointed out above, there is unity of invention among Groups I-VI and XI because the special technical feature common to these groups is an association of certain RUP41 polypeptides and variants thereof with cardioprotection. Such an association defines a contribution over the prior art. Therefore, for this reason Groups I-VI and XI should be rejoined.

Applicants also respectfully urge the Examiner to rejoin the claims of Groups II-VI and XI with the claims of elected Group I for examination in this application for the following additional reasons:

The MPEP allows an Examiner to examine otherwise patentably distinct sets of claims if to do so would not impose an undue burden on the Examiner. MPEP § 803 states (emphasis added) that:

> **If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.**

In the present case, by virtue of the special technical feature common to Groups I-VI and XI, elements of the non-elected groups are found in the claims of elected Group I. For example, the claims of Group V are directed a method of preparing a composition using the modulator identified as cardioprotective according to the method of the claims of Group I.

As such, it is believed that the search for the claims of Group I will uncover any relevant prior art relating to the claims of non-elected groups II-VI and XI. Accordingly, little if any additional searching

should be required for the claims of these non-elected groups with elected Group I. Therefore, the examination of the claims of non-elected groups II-VI and XI together with the claims of elected Group I should impose little if any additional burden on the Examiner.

Consequently, examining the claims of non-elected groups II-VI and XI and the claims of elected Group I together in the present application clearly does not impose an undue or **serious burden** on the Examiner. In the absence of such an undue or serious burden, the Examiner is clearly instructed by the MPEP to examine the entire application. Applicants are requesting rejoinder only of those Groups that can be searched without serious additional search burden. Therefore, the Examiner is respectfully requested to rejoin the claims of non-elected groups II-VI and XI with the claims of elected Group I and to examine together all the claims of these groups in the present application.

Groups VII and VIII should be rejoined with each other because unity of invention is present among claims to the product (knockout mouse or rat), to the method of making a knockout mouse or rat, and to the method of using the knockout mouse or rat. This is so because the knockout mouse or rat is a special technical feature common to all these claims.

Similarly, Groups XIII and XIV should be rejoined with each other because unity of invention is present between claims to the product (transgenic non-human animal) and to the method of using the transgenic non-human animal. This is so because the transgenic non-human animal is a special technical feature common to these claims.

Conclusion

In summary, Applicants respectfully urge the Examiner to withdraw the election of species requirements and to reformulate the groupings of claims subject to the restriction requirement in accordance with proper unity of invention practice.

If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number AREN-007.

Respectfully submitted,
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